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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/525,006

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Shirou Sawa

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EXAMINER

JAGOE, DONNA A

ART UNIT

PAPER NUMBER

1619

MAIL DATE

DELIVERY MODE

12/24/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/525,006	Applicant(s) SAWA ET AL.	
	Examiner Donna Jagoe	Art Unit 1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 October 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-29,31-34,36-51,53-56 and 58-63 is/are pending in the application.
- 4a) Of the above claim(s) 39,40,61 and 62 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-29,31-34,36-38,41-51,53-56,58-60 and 63 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 5, 2009 has been entered.

Claims 19-29, 31-34, 36-51, 53-56 and 58-63 are pending in this application.

Claims 39, 40, 61 and 62 are withdrawn from further consideration.

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are rejected.

Priority

Receipt is acknowledged of the Japanese priority application and certified translation submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellberg et al. (US 5,998,465; 1999) and Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenac in rodents; Agents and Actions; 1988 Aug; 25(1-2):77-85; cited with previous Interview Summary).

Hellberg teaches pharmaceutical compositions of anti-inflammatory compounds (abstract); the compounds include a non-steroidal anti-inflammatory moiety (NSAIA) and an antioxidant moiety linked through an ester bond formed by the carboxylic acid moiety of the NSAIA (col. 2, lines 20-24); NSAIA moieties include bromfenac (col. 3, line 57; claim 5); examples 2 and 3 (col. 11) teach topical ophthalmic formulations useful for treating inflammation, both of these formulations include tyloxapol at 0.01-0.05 w/v %, HPMC (thickener), benzalkonium chloride (preservative), edetate disodium (chelating agent) (col. 11, Examples 2-3); the pH is adjusted to 7.4 (about 7.5; col. 11, line 64); topical formulations administered by drops (eye drops; col. 10, lines 15-18). Hellberg does not teach bromfenac (only the ester of bromfenac). Nolan teaches bromfenac (the sodium salt, sesquihydrate form) was effective as a topical analgesic at concentrations of 0.1-0.32 % in mice and more potent than the other drugs tested (abstract). It would have been obvious for one of ordinary skill in the art at the time of the invention to substitute bromfenac, taught by Nolan for the compounds of Hellberg in the example formulation giving formulations of the instant claims and to select concentrations of bromfenac sodium, sesquihydrate of 0.1, about 0.2 and about 0.32 %, in the invention of Gamache, since these values have demonstrated efficacy for topical use. It would

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also have been obvious to adjust the concentration of tyloxapol, to optimize the formulations for the effect would on the solubility and stability of the aqueous preparations, which would have resulted in the effective tyloxapol concentrations of about 0.02 and 0.3 w/v%, recited in claims 25 and 32. The motivation to substitute bromfenac in the Hellberg formulations would have been the art-recognized equivalent activity of bromfenac as an anti-inflammatory agent in topical usage. The motivation to adjust concentrations would have been the routine optimization of these topical ophthalmic formulations for anti-inflammatory use in the eye.

Claims 19-29, 31-34 and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gamache, et al. (WO 01/15677 A2; 03/2001; previously cited) and ISTA Pharmaceuticals ("New Drug Applications: Xibrom", http://www.drugs.com/nda/xibrom_040525.html, accessed online 9/19/2007; previously cited) or Nolan, et al. ("The topical anti-inflammatory and analgesic properties of bromfenac in rodents; Agents and Actions; 1988 Aug; 25(1-2):77-85; provided with Interview Summary).

Gamache teaches compositions for otic and intranasal use (p.6, lines 5-6) that contain a combination of a 5-HT agonist and an anti-inflammatory agent (p. 6, lines 1-4; p. 12 lines 9-10) or alternatively sequential or concurrent dosing of separate compositions that contain the 5-HT antagonist in one composition and the anti-inflammatory agent in a second composition (p. 12, lines 9-11); specifically claimed is the anti-inflammatory specie bromfenac (2-amino-3-(4-bromobenzoyl)phenylacetic

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acid). Typical concentrations of anti-inflammatory agents, such as bromfenac, are taught in the range 0.01-1.0 % (w/v) (overlapping with 0.01-0.5; p. 13, lines 6-8); aqueous formulations are preferred (p. 10, lines 11-14); tyloxapol is taught in a concentration of 0.05 % (w/v) (p. 16, line 30). It is noted that instant claim 21 and further dependent claims limit the options for the salt of bromfenac to the sodium salt, and that the specific concentrations recited in dependent claims apply to the sodium salt; the other options (bromfenac or a hydrate of bromfenac) are still viable choices that are part of instant claim 21 claims depending therefrom (which depend on and include the options of claim 20). Gamache teaches bromfenac in the concentration range of claim 20 (which is also an option of claims 21-24 and 31). The salt form of bromfenac in solution will be the same when the acid is dissolved in a solution followed by adjustment to the desired pH with NaOH/HCl (Gamache, p. 15, line 33) as when the sodium salt is dissolved in solution adjusted to the same pH; in this case Gamache also teaches the sodium salt limitation of instant claim 21, albeit not the sodium salt concentration limitation of instant claim 22 and further dependent claims, since the claim is drawn to an aqueous liquid preparation, irrespective of how it is prepared. However, the concentration range of 0.01-1.0% overlaps and encompasses the claimed concentration range of the sodium salt of bromfenac instantly claimed.

The ISTA Pharmaceuticals news release demonstrates that products containing 0.1 % bromfenac sodium acquired US marketing rights for Xibrom in May 2002 (were known by others in this country before applicant's priority date, a 35 USC 102(a) date). Nolan teaches bromfenac (the sodium salt, sesquihydrate form) was effective as a

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topical analgesic at concentrations of 0.1-0.32 % in mice and more potent than the other drugs tested (abstract). It would have been obvious for one of ordinary skill in the art at the time of the invention to select concentrations of bromfenac sodium, sesquihydrate of 0.1, about 0.2 and about 0.32 %, in the invention of Gamache, since these values have demonstrated efficacy for topical use. It would have been obvious to adjust the concentration of tyloxapol, to see what the effect would be on the solubility and stability of the aqueous preparations, which would have resulted in the effective concentrations of the instant claims. It would also have been obvious to adjust the pH to values in the 7.5 to 8.5 range, with the potential of dissolving and/or stabilizing more of the acidic drug, bromfenac, in a more aqueous soluble ionic form. The motivation would have been to prepare pharmaceutical products with optimal drug dosage and stability.

Double Patenting

Claims 19-29, 31-34, 36-38, 41-51, 53-56, 58-60 and 63 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-43 of copending Application No. 11/755662.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application contains claims drawn to method of treating pain and/or inflammation associated with an ocular condition, by administering the aqueous solutions of the instant claims. It would have been obvious to one of ordinary skill in the art at the time of the invention to use the formulations of the instant claims in the methods of the copending application, since the claims recite that the

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formulations are eye drops, and the instant abstract also teaches some of the conditions treated of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/YVONNE L. EYLER/
Supervisory Patent Examiner, Art Unit 1619

Donna Jagoe /D. J./
Examiner
Art Unit 1619

December 17, 2009